

## STN- Structure

Search  
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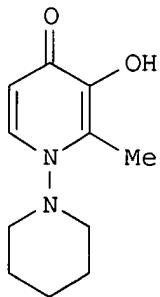
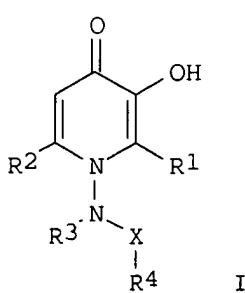
10/803,724

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L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:633411 CAPLUS  
 DOCUMENT NUMBER: 139:179975  
 TITLE: Preparation of N-substituted 3-hydroxy-4-pyridinones  
 and metal chelates as pharmaceuticals  
 INVENTOR(S): Liu, Shuang  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003065991	A2	20030814	WO 2003-US3375	20030205
WO 2003065991	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003170174	A1	20030911	US 2003-358835	20030205
US 6825204	B2	20041130		
EP 1474396	A2	20041110	EP 2003-737635	20030205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004176326	A1	20040909	US 2004-803724	20040318
PRIORITY APPLN. INFO.:			US 2002-354339P	P 20020205
			US 2003-358835	A3 20030205
			WO 2003-US3375	W 20030205

OTHER SOURCE(S): MARPAT 139:179975  
 GI



AB N-substituted 3-hydroxy-4-pyridinones of formula I [X = CH<sub>2</sub>, CO, CS, P(O)dialkyl, SO<sub>2</sub>, C(NH)NH, CONH, CSNH; R<sub>1</sub>, R<sub>2</sub> = H, alkyl, aryl, heteroaryl, etc.; R<sub>3</sub>, R<sub>4</sub> = alkyl, aryl, heteroaryl, etc.; R<sub>3</sub>R<sub>4</sub> = alkylene, heteroalkylene] and metal chelates are prepared. The N-substituted 3-hydroxy-4-pyridinones and their metal chelates are used as

pharmaceutical agents for the treatment of diseases, such as parasitic and viral infections, conditions associated with inflammation and infection, and conditions mediated by cell-proliferation or collagen formation, or as radiopharmaceuticals and MRI contrast agents. Thus, II was prep'd from maltol and 1-aminopiperidine, then chelated with  $^{111}\text{InCl}_3$ .

IT 577973-72-9P 577973-73-0P 577973-74-1P

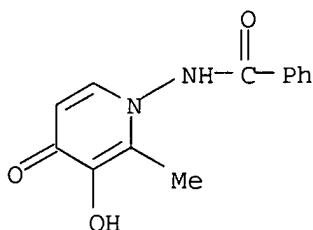
577973-75-2P 577973-76-3P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxypyridinones and metal chelates as pharmaceuticals)

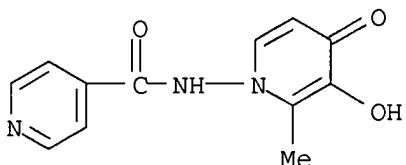
RN 577973-72-9 CAPLUS

CN Benzamide, N-(3-hydroxy-2-methyl-4-oxo-1(4H)-pyridinyl)- (9CI) (CA INDEX NAME)



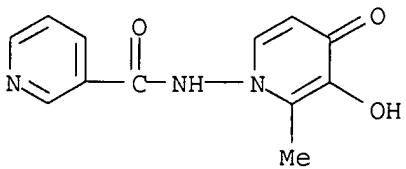
RN 577973-73-0 CAPLUS

CN 4-Pyridinecarboxamide, N-(3-hydroxy-2-methyl-4-oxo-1(4H)-pyridinyl)- (9CI) (CA INDEX NAME)



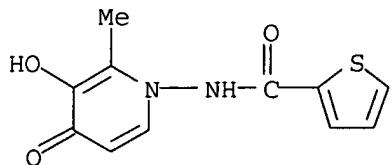
RN 577973-74-1 CAPLUS

CN 3-Pyridinecarboxamide, N-(3-hydroxy-2-methyl-4-oxo-1(4H)-pyridinyl)- (9CI) (CA INDEX NAME)

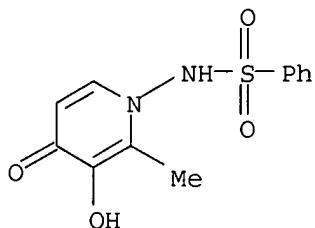


RN 577973-75-2 CAPLUS

CN 2-Thiophenecarboxamide, N-(3-hydroxy-2-methyl-4-oxo-1(4H)-pyridinyl)- (9CI) (CA INDEX NAME)



RN 577973-76-3 CAPLUS

CN Benzenesulfonamide, N-(3-hydroxy-2-methyl-4-oxo-1(4H)-pyridinyl)- (9CI)  
(CA INDEX NAME)

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:887972 CAPLUS

DOCUMENT NUMBER: 123:285638

TITLE: Preparation of cephem derivatives as antibacterials

INVENTOR(S): Sendai, Michuki; Nakao, Masafumi; Ishibashi, Yukio

PATENT ASSIGNEE(S): Takeda Chemical Industries Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.

CODEN: JKXXAF

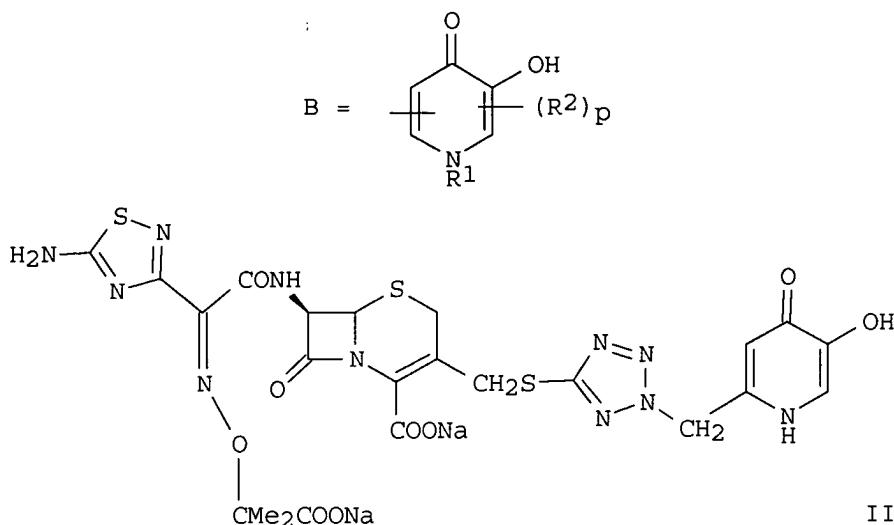
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07179474	A2	19950718	JP 1994-268316	19941005
PRIORITY APPLN. INFO.:			JP 1993-274945	A 19931005
OTHER SOURCE(S):	MARPAT	123:285638		
GI				



AB Cephems substituted at the 3 position with the group -CH<sub>2</sub>-S-A-Y-B [A = (un)substituted bivalent aromatic radical; R1 = H, (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted amino; R2 = OH, (un)substituted alkyl, (un)substituted alkoxy; p = 0, 1, 2; the OH may be protected; Y = bond, S, O, NH, CONH, or bivalent hydrocarbyl radical] are prepared. Thus, sodium 7 $\beta$ -[2-(5-amino-1,2,4-thiadiazol-3-yl)-(Z)-2-[[[1-(4-methoxybenzyloxy carbonyl)-1-methylethoxy]imino]acetamido]-3-(hydroxymethyl)-3-cephem-4-carboxylate was reacted with 5-mercaptop-2-[[5-(4-methoxybenzyloxy)-4-pyridon-2-yl]methyl]-2H-tetrazole in DMF containing o-phenylene phosphate at room temperature for 2 h followed by treatment with CF<sub>3</sub>CO<sub>2</sub>H to give the title compound I. In an in vitro study this had an MIC of 0.2  $\mu$ g/mL against *Pseudomonas aeruginosa*.

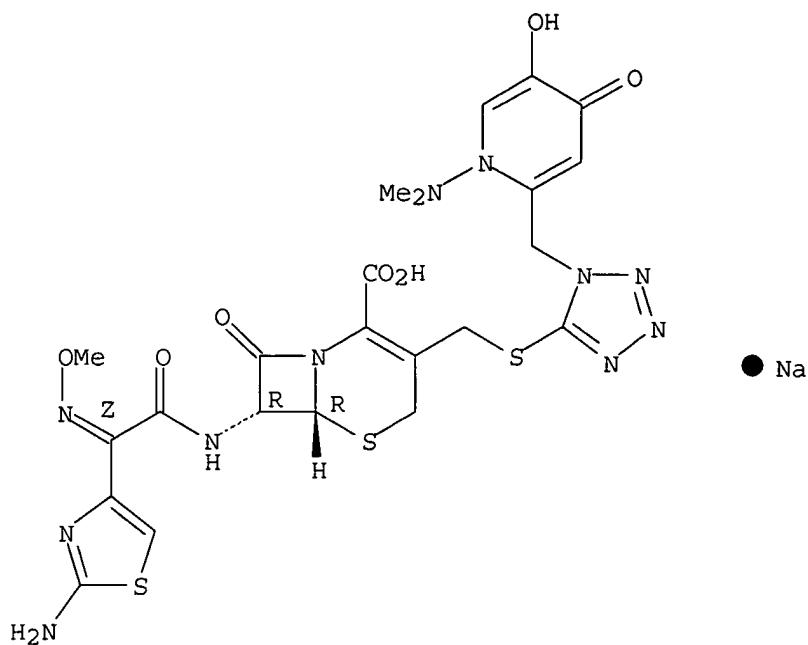
IT **169552-11-8P 169552-12-9P 169552-13-0P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of cephem derivs. as antibacterials)

RN 169552-11-8 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
7-[[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[[1-[[1-  
(dimethylamino)-1,4-dihydro-5-hydroxy-4-oxo-2-pyridinyl]methyl]-1H-  
tetrazol-5-yl]thio]methyl]-8-oxo-, monosodium salt, [6R-  
[6 $\alpha$ ,7 $\beta$ (Z)]]- (9CI) (CA INDEX NAME)

## Absolute stereochemistry

Double bond geometry as shown.

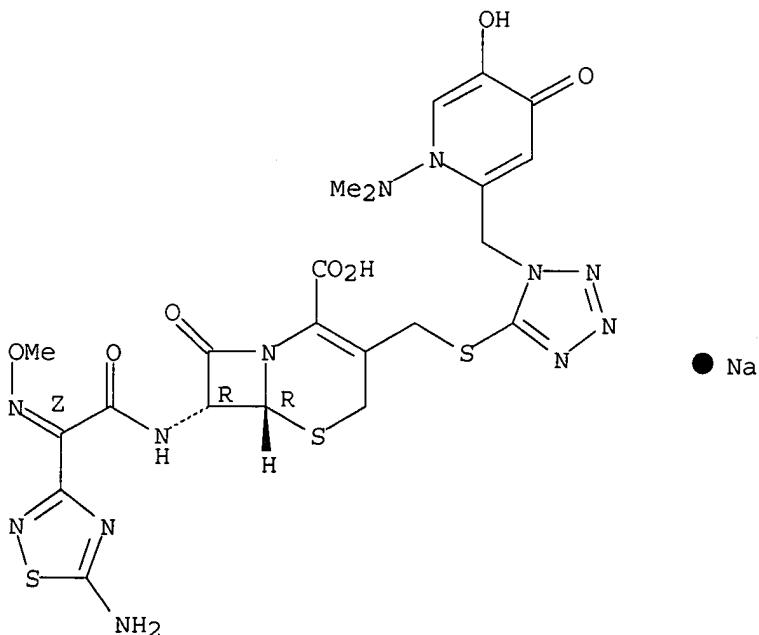


RN 169552-12-9 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 7-[[[(5-amino-1,2,4-thiadiazol-3-yl)(methoxyimino)acetyl]amino]-3-[[[[1-  
 (dimethylamino)-1,4-dihydro-5-hydroxy-4-oxo-2-pyridinyl]methyl]-1H-  
 tetrazol-5-yl]thio]methyl]-8-oxo-, monosodium salt, [6R-  
 [6 $\alpha$ ,7 $\beta$ (Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

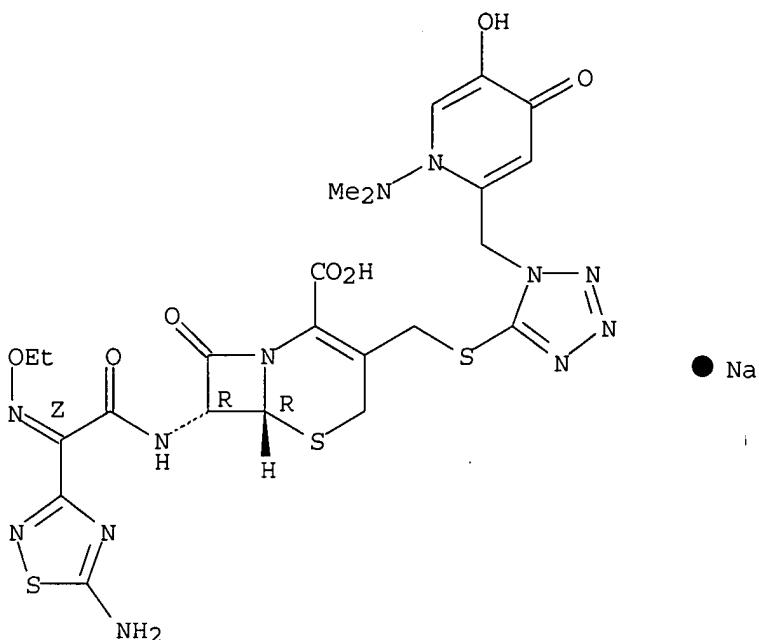
Double bond geometry as shown.



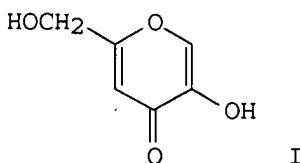
RN 169552-13-0 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
7-[[[(5-amino-1,2,4-thiadiazol-3-yl)(ethoxyimino)acetyl]amino]-3-[[[1-[(dimethylamino)-1,4-dihydro-5-hydroxy-4-oxo-2-pyridinyl]methyl]-1H-tetrazol-5-yl]thio]methyl]-8-oxo-, monosodium salt, [6R-[6 $\alpha$ ,7 $\beta$ (Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1990:77740 CAPLUS  
DOCUMENT NUMBER: 112:77740  
TITLE: Heterocycles from carbohydrate precursors.  
Perspectives and mechanistic aspects of the action of  
hydrazines on kojic acid  
AUTHOR(S): El Ashry, El Sayed H.; El Kilany, Yeldez; Mousaad,  
Ahmed  
CORPORATE SOURCE: Fac. Sci., Alexandria Univ., Alexandria, Egypt  
SOURCE: Journal of Carbohydrate Chemistry (1989), 8(3), 485-95  
CODEN: JCACDM; ISSN: 0732-8303  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 112:77740  
GI

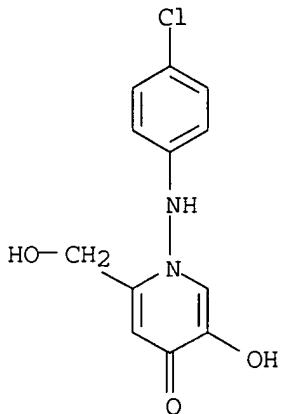


AB The mode of action of arylhydrazines on kojic acid (I) was investigated. Some novel types of compds. were isolated, and their structures were determined. The mechanism of the reactions is discussed.

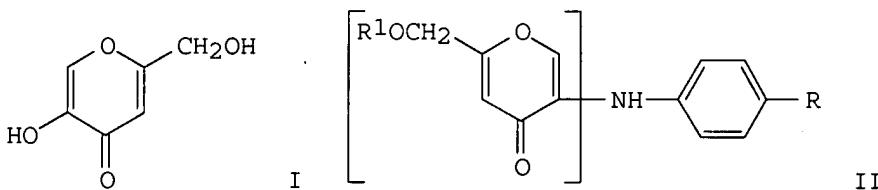
IT 103596-93-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 103596-93-6 CAPLUS

CN 4(1H)-Pyridinone, 1-[(4-chlorophenyl)amino]-5-hydroxy-2-(hydroxymethyl)-  
 (9CI) (CA INDEX NAME)



L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1986:478852 CAPLUS  
 DOCUMENT NUMBER: 105:78852  
 TITLE: Reaction of kojic acid with arylhydrazines  
 AUTHOR(S): El Ashry, El Sayed H.; El Kilany, Yeldez; Mousaad, Ahmed  
 CORPORATE SOURCE: Fac. Sci., Alexandria Univ., Alexandria, Egypt  
 SOURCE: Acta Pharmaceutica Jugoslavica (1986), 36(1), 73-4  
 DOCUMENT TYPE: CODEN: APJUA8; ISSN: 0001-6667  
 LANGUAGE: Journal  
 OTHER SOURCE(S): English  
 GI: CASREACT 105:78852

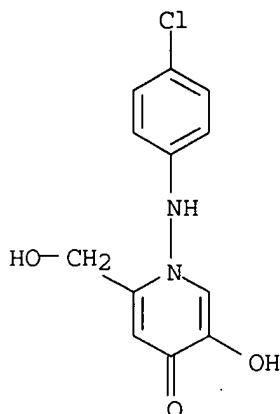


AB Reaction of kojic acid (I) with p-bromo- or p-chlorophenylhydrazine gave rise to a number of products. One of them was II (R = Br; R<sup>1</sup> = H) the structure of which was confirmed by detailed NMR anal. The Cl analog II (R = Cl; R<sup>1</sup> = H) gave similar NMR spectra and on acetylation gave II (R = Cl; R<sup>1</sup> = Ac), thus confirming the structure. Other products obtained from the reaction are described.

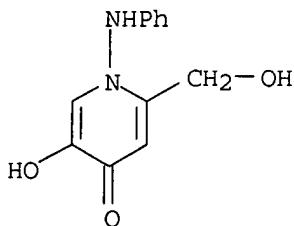
IT 103596-93-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)

10/803, 724

(preparation of)  
RN 103596-93-6 CAPLUS  
CN 4(1H)-Pyridinone, 1-[(4-chlorophenyl)amino]-5-hydroxy-2-(hydroxymethyl)-  
(9CI) (CA INDEX NAME)

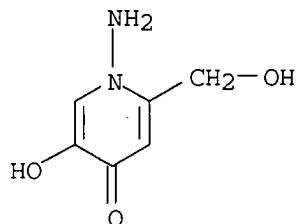


L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1974:491412 CAPLUS  
DOCUMENT NUMBER: 81:91412  
TITLE: Mode of action of phenylhydrazine on kojic acid  
AUTHOR(S): El Ashry, El Sayed H.  
CORPORATE SOURCE: Fac. Sci., Alexandria Univ., Alexandria, Egypt  
SOURCE: Carbohydrate Research (1974), 33(1), 178-83  
CODEN: CRBRAT; ISSN: 0008-6215  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Treating kojic acid (I) with 20 ml PhNH<sub>2</sub> (II) in AcOH 1 hr at 100° gave isomeric 3-hydroxymethyl-5-(2-hydroxy-1-oxoethyl)-1-phenylpyrazole phenylhydrazone, 5-(1,2-dioxoethyl)-3-(hydroxymethyl)-1-phenylpyrazole bis(phenylhydrazone), 1-anilino-5-hydroxy-2-(hydroxymethyl)-4-pyridinone and an un-identified adduct of I and II. Structures were established by oxidative degradation and by NMR and mass spectrometry.  
IT 54345-81-2P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and mass spectrum of)  
RN 54345-81-2 CAPLUS  
CN 4(1H)-Pyridinone, 5-hydroxy-2-(hydroxymethyl)-1-(phenylamino)- (9CI) (CA INDEX NAME)



L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1961:8151 CAPLUS  
DOCUMENT NUMBER: 55:8151

ORIGINAL REFERENCE NO.: 55:1641i,1642a-c  
 TITLE: Reactions of kojic acid with hydrazine  
 AUTHOR(S): Marxer, A.; Thomas, A. F.  
 CORPORATE SOURCE: CIBA Akt.-Ges., Basel, Switz.  
 SOURCE: Chimia (1960), 14, 126-7  
 CODEN: CHIMAD; ISSN: 0009-4293  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German  
 AB Free kojic acid (I) reacts with hydrazine (II) via an intermediate opening of the pyran ring and subsequent closure in the 2-5 positions to form 3,6-bis(hydroxymethyl)-4(1H)-pyridazinone, along with the hydrazone of (3-hydroxymethyl-5-pyrazolyl)hydroxyacetaldehyde resulting from inclusion of II between positions 2 and 4. The hydroxypyrazole, which could result from addition of II to positions 4 and 6 of the same intermediate, cannot be detected. If both (or only the acid) OH groups of I are blocked by etherification, II effects ring closure by reaction with positions 2 and 6, yielding ethers of 2-hydroxymethyl-5-hydroxy-N-amino-4-pyridinone, and also by reaction between positions 2 and 4, yielding a hydrazone of an etherified pyrazolylacetaldehyde (but not by reaction with positions 4 and 6). Neither a diazepinone nor a bis-pyridinone can be found. I reacts with phenylhydrazine (or methylhydrazine) to yield a red crystalline compound (suggested structure, 2-hydroxymethyl-5-phenylazo-N-phenylamino-4-pyridinone), along with the phenylhydrazone of (1-phenylpyrazolyl)hydroxyacetaldehyde.  
 IT 98135-05-8, 4(1H)-Pyridone, 1-amino-5-hydroxy-2-(hydroxymethyl)- (derivs.)  
 RN 98135-05-8 CAPLUS  
 CN 4(1H)-Pyridone, 1-amino-5-hydroxy-2-(hydroxymethyl)- (6CI) (CA INDEX NAME)



L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1960:97564 CAPLUS  
 DOCUMENT NUMBER: 54:97564  
 ORIGINAL REFERENCE NO.: 54:18500i,18501a-i,18502a-g  
 TITLE: Chemotherapeutic studies in the heterocyclic series.  
 XXX. Reaction of kojic acid with hydrazine. 2.  
 Reaction of kojic acid ethers with hydrazine  
 AUTHOR(S): Thomas, A. F.; Marxer, A.  
 CORPORATE SOURCE: C I B A Ltd. Basel, Switz.  
 SOURCE: Helvetica Chimica Acta (1960), 43, 469-77  
 CODEN: HCACAV; ISSN: 0018-019X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German  
 OTHER SOURCE(S): CASREACT 54:97564  
 GI For diagram(s), see printed CA Issue.  
 AB cf. CA 54, 12133h. The reaction of kojic acid (I) 5-mono- and  $\alpha$ ,5-diethers with  $N_2H_4 \cdot H_2O$  (II) gave the corresponding 1-amino-4-pyridinones, as well as 1 of the 2 possible pyrazole derivs. The structures of the compds. were discussed. (corrected m.ps. given).  $Me_2SO_4$  (126 g.) added dropwise during 1 hr. to 142 g. I in 620 ml. 10% aqueous KOH

with stirring (occasional cooling to keep the temperature below 25°), after 1 hr. the mixture treated with an addnl. 620 ml. 10% aqueous KOH, 126 g. Me<sub>2</sub>SO<sub>4</sub> added dropwise at room temperature, the mixture heated slowly to 50°, allowed to cool to room temperature, treated with 310 ml. 10% aqueous KOH and then with 63 g. Me<sub>2</sub>SO<sub>4</sub>, heated to 50°, allowed to stand overnight, made strongly alkaline with solid KOH, extracted with CHCl<sub>3</sub>, and the extract evaporated gave 94 g. O.C(CH<sub>2</sub>OMe):CH.CO.C(OMe):CH (III), m. 90-1° (PhMe). III (34 g.), 24 ml. II, and 100 ml. MeOH refluxed 30 min., the mixture concentrated somewhat, diluted with Et<sub>2</sub>O, and the crude product recrystd.

from EtOH and a little Et<sub>2</sub>O gave 4.5 g. H<sub>2</sub>NN.C(CH<sub>2</sub>OMe):CH.CO.C(OMe):CH (IV), m. 183-5°; picrate m. 164-6° (aqueous EtOH). The mother liquor from III evaporated to dryness, the residue (28 g.) dissolved in 300 ml. MeOH, the solution treated with NH<sub>3</sub> during 2-3 min., the mixture hydrogenated at 70 atmospheric and 90° with 3-4 g. Raney Ni (4700 ml. H absorbed), filtered, the filtrate evaporated, and the residue distilled in vacuo

gave 15 g. NH.N:C(CH<sub>2</sub>OMe).CH:CCH(OMe)CH<sub>2</sub>NH<sub>2</sub> (V), b<sub>0</sub>.3 170°; dioxalate m. 94-6° (EtOH-EtOAc). V (1.5 g.) and 10 g. KMnO<sub>4</sub> in 75 ml. H<sub>2</sub>O heated 2 hrs. on a H<sub>2</sub>O bath, the mixture filtered, the filtrate concentrated somewhat, treated with concentrated HCl, and the precipitate recrystd. from H<sub>2</sub>O

gave NH.N:C(CO<sub>2</sub>H).CH:CCO<sub>2</sub>H (VI), m. 295-7° (decomposition). IV (1.6 g.) in 10 ml. C<sub>5</sub>H<sub>5</sub>N treated with 1 ml. Ac<sub>2</sub>O, the mixture heated until complete solution occurred, the solution allowed to stand overnight at room temperature, evaporated, and the product recrystd. from Me<sub>2</sub>CO gave the 1-Ac derivative of

IV,

m. 207°. I (14.2 g.) and 13 ml. PhCH<sub>2</sub>Cl added to 2.3 g. Na dissolved in 200 ml. MeOH, the mixture refluxed 3 hrs., poured into 1 l. H<sub>2</sub>O, and the resulting precipitate recrystd. from EtOH gave 22 g. O.C(CH<sub>2</sub>OH):CH.CO.C(OCH<sub>2</sub>Ph):CH (VII), m. 133°. VII (35 g.) and 18.3 ml. II in 250 ml. MeOH refluxed 30 min., concentrated somewhat, diluted with Et<sub>2</sub>O,

and the product recrystd. from EtOH gave 6 g. H<sub>2</sub>NN.C(CH<sub>2</sub>OH):CH.CO.C(OR):CH (VIII) (R = CH<sub>2</sub>Ph) (IX), m. 174°. The mother liquor from IX concentrated, allowed to stand several weeks, the precipitate (12 g.) washed with EtOH,

and recrystd. twice from MeOH-Et<sub>2</sub>O gave NH.N:C(CH<sub>2</sub>OH).CH:CCH(OCH<sub>2</sub>Ph)CH:NNH<sub>2</sub> (X), m. 150-2°. X oxidized with aqueous KMnO<sub>4</sub> as above, the product sublimed at 110°/15 mm. (BzOH sublimed), and the residue recrystd. from H<sub>2</sub>O gave VI. IX (1.6 g.) treated with 1.8 g. (EtCO)<sub>2</sub>O in C<sub>5</sub>H<sub>5</sub>N and the product recrystd. from EtOH gave 1,2-di-EtCO derivative of IX, m. 154-5°. IX (4.6 g.) hydrogenated with 2% Pd-C in EtOH (415 ml. H absorbed in 38 min.), the catalyst filtered off, extracted with boiling EtOH, and the combined EtOH solns. concentrated somewhat and cooled gave 2.48 g. VIII (R = H), m. 239-48° (EtOH). IX (3.5 g.) treated with 6 ml. SOCl<sub>2</sub>, after 2 hrs. the unreacted SOCl<sub>2</sub> washed out with petr. ether, and the product recrystd. from EtOH gave 4.0 g. crude H<sub>2</sub>NN.C(CH<sub>2</sub>Cl):CH.CO.C(OCH<sub>2</sub>Ph):CH (XI) HCl salt (XII), m. 209° (EtOH). Na<sub>2</sub>CO<sub>3</sub> (2N) added to aqueous XII at 50° gave XI, m. 157° (EtOH-petr. ether). O.C(CH<sub>2</sub>Cl):CH.CO.C(OH):CH (Yabuta, CA 18, 1665) (45 g.) hydrogenated in MeOH with 5 g. Pd-C in the presence of 40 g. NaOAc (after absorption of 6650 ml. H, the hydrogenation was terminated), the mixture filtered, the filtrate treated with 12.6 g. Na in 120 ml. MeOH and 35 g. PhCH<sub>2</sub>Cl, the mixture refluxed 4 hrs., concentrated, diluted with 1.5

1.

H<sub>2</sub>O, and the product isolated (after adding EtOAc) gave 45 g. crude O.CMe:CH.CO.C(OCH<sub>2</sub>Ph):CH (XIII), anal. sample m. 89-90° (petr. ether). XIII (10.5 g.), 6 ml. I, and 50 ml. MeOH refluxed 1 hr. and diluted with EtOAc gave 2 g. H<sub>2</sub>NN.CMe:CH.CO.C(OR):CH (XIV) (R = CH<sub>2</sub>Ph) (XV), m. 195° (decomposition) (EtOH-EtOAc); acetate m. 206° (EtOH-Et<sub>2</sub>O). XIII (1.1 g.) and 3 g. NaOAc in 30 ml. EtOH and 30 ml. AcOH hydrogenated

over 0.3 g. Pd-C (185 ml. H absorbed), the mixture concentrated, the residue extracted

(Soxhlet) with EtOAc, and the extract allowed to stand gave 300 mg. XIV (R = H) (XVI), m. 248-50° (EtOH-EtOAc). XV (340 mg.) hydrogenated over Pd-C in EtOH gave XVI. IX (2.46 g.) suspended in 50 ml. EtOH and 50 ml. 2N HCl, the mixture treated dropwise at 0° with 0.75 g. NaNO<sub>2</sub> in 10 ml. H<sub>2</sub>O with stirring (vibromixer), the solution brought slowly to room temperature, after 2 hrs. neutralized with aqueous NH<sub>3</sub>, and the precipitate (2.15 g.)

filtered off and crystallized (EtOH) gave  $\text{NH.C(CH}_2\text{OH):CH.CO.C(OR):CH}$  (XVII) ( $\text{R} = \text{CH}_2\text{Ph}$ ) (XVIII), m. 224-6°. VII (10 g.) dissolved in 100 ml. concentrated aqueous  $\text{NH}_3$  and 20 ml. EtOH, the solution refluxed 5 hrs.

(evaporated NH<sub>3</sub>)

occasionally replaced), and the precipitate (9 g.) filtered off and recrystd. (EtOH) gave XVIII. XVIII (from either preparation) (2 g.) in EtOH shaken with H over 10% Pd-C (after 15 min. 205 ml. H absorbed), the catalyst filtered off, extracted several times with boiling EtOH, the combined filtrates concentrated,

and the residue (0.98 g.) recrystd. from MeOH gave XVII (R = H), m. 246° (decomposition). IX (0.5 g.) and 0.25 g. BzH in 20 ml. MeOH refluxed 15 min., treated with a drop of Ac<sub>2</sub>O, the solution refluxed an addnl. 2 hrs., diluted with H<sub>2</sub>O, the precipitated oil allowed to stand 24 hrs. and

the resulting solid (0.3 g.) crystallized twice from aqueous EtOH gave R':NN.C(CH<sub>2</sub>OH):CH.CO.C(OR):CH (XIX) (R = CH<sub>2</sub>Ph, R' = CHPh) (double m.p. 110° and 171-3°). IX (0.5 g.) and 0.32 g. 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CHO (XX)

in 10 ml. AcOH refluxed 4 hrs., concentrated, the residue rubbed with 50% aqueous EtOH, and the solid (0.6 g.) crystallized from EtOH and MeOH gave XIX ( $R = CH_2Ph$ ,  $R' = CHC_6H_4NO_2-4$ ), m. 184-5°. XVI (0.3 g.) and 0.32 g. XX in 10 ml. AcOH refluxed 2 hrs., the solution scratched, and the precipitate (0.4 g.)

filtered off and crystallized (N-methylpyrrolidone-EtOH) gave 4-O2NC6H4CH:NN.CMe:CH.CO.C(OH):CH, m. 259° (decomposition). V dibenzoate (Yabuta, CA 17, 1475) (7.0 g.) and 2.2 ml. II in 175 ml. MeOH boiled 1 hr., the solution evaporated, and the residue recrystd. twice from

EtOH       $\text{S}_1 \text{S}(\text{CH}_2\text{CH}_3) \rightarrow \text{CH}_3\text{CH}_2\text{S}(\text{CH}_3) \text{CH}_3$       101.21

gave  $O.C(CH_2OBz)_2 : CH \cdot CO \cdot C(OH) : CH$ , m. 181-2°.

98134-90-8, 4-(1H)-Pyridone, 1-amino-5-hydroxy-2-methyl-  
98135-25-8, 4-(1H)-Pyridone, 1-amino-5-hydroxy-3-(hydroxymethyl)-

98135-05-8, 4(1H)-Pyridone, 1-amino-5-hydroxy-2-(hydroxymethyl)-; 100238-50-5, 4(1H)-Pyridone, 5-hydroxy-2-methyl-1-(methylsulfonyl)-

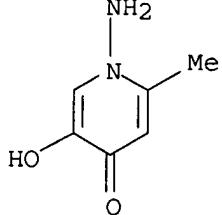
100728-50-5, 4(1H)-Pyridone, 5-hydroxy-2-methyl-1-(p-nitrobenzylideneamino)-

### Microbenzyridineamino - (preparation of)

(preparation 31)

RN 58154-50-8 CAFES  
CN 4 (1H)-Pyridone 1-

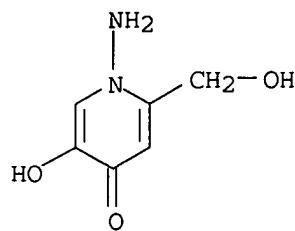
CN 4-(1H)-Pyridone, 1-amino-3-hydroxy-2-methyl- (8CI) (CA INDEX NAME)



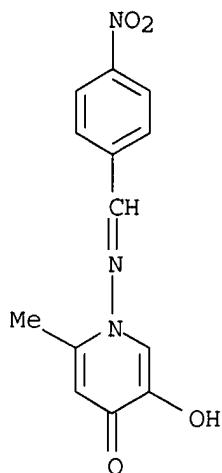
RN 98135-05-8 CAPLUS

CN 4 (1H) - Pyridone, 1-amino-5-hydroxy-2-(hydroxymethyl) - (6CI) (CA INDEX NAME)

10/803,724



RN 100728-50-5 CAPLUS  
CN 4 (1H) - Pyridone, 5-hydroxy-2-methyl-1-(p-nitrobenzylideneamino) - (6CI) (CA  
INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 11:43:11 ON 04 FEB 2005)

FILE 'REGISTRY' ENTERED AT 11:43:23 ON 04 FEB 2005

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L2 0 S L1  
L3 STRUCTURE UPLOADED  
L4 1 S L3  
L5 16 S L3 FULL

FILE 'CAPLUS' ENTERED AT 11:45:10 ON 04 FEB 2005

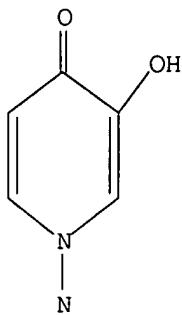
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L3 HAS NO ANSWERS

L3 STR

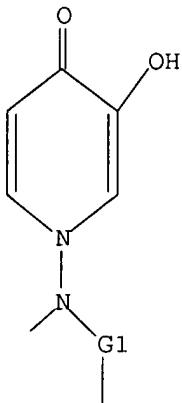
10/803, 724



G1 C, S, P

Structure attributes must be viewed using STN Express query preparation.

=> d 11  
L1 HAS NO ANSWERS  
L1 STR



G1 C, S, P

Structure attributes must be viewed using STN Express query preparation.

=>

Day : Friday  
 Date: 2/4/2005  
 Time: 11:47:25


**PALM INTRANET**
**Inventor Name Search Result**

Your Search was:

Last Name = LIU

First Name = SHUANG

Application#	Patent#	Status	Date Filed	Title	Inventor Name 51
<a href="#"><u>60588448</u></a>	Not Issued	020	07/15/2004	ARYL- AND HETEROARYL-SUBSTITUTED TETRAHYDROISOQUINOLINES AND USE THEREOF TO BLOCK REUPTAKE OF NOREPINEPHRINE, DOPAMINE, AND SEROTONIN	LIU, SHUANG
<a href="#"><u>60543176</u></a>	Not Issued	020	02/10/2004	CROWNED DITHIOCARBAMATE METAL COMPLEX PHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>60494959</u></a>	Not Issued	159	08/13/2003	SUBSTITUTED PYRIDINONES	LIU, SHUANG
<a href="#"><u>60478462</u></a>	Not Issued	159	06/13/2003	CHELANTS AND MACROCYCLIC METAL COMPLEX RADIOPHARMACEUTICALS THEREOF	LIU, SHUANG
<a href="#"><u>60478458</u></a>	Not Issued	159	06/13/2003	CHELANTS AND MACROCYCLIC METAL COMPLEX RADIOPHARMACEUTICALS THEREOF	LIU, SHUANG
<a href="#"><u>60354339</u></a>	Not Issued	159	02/05/2002	N-SUBSTITUTED 3-HYDROXY-4-PYRIDINONES AND PHARMACEUTICALS CONTAINING THEREOF	LIU, SHUANG
<a href="#"><u>60271389</u></a>	Not Issued	159	02/26/2001	ASCORBIC ACID ANALOGS STABILIZERS FOR METALLORADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>60260618</u></a>	Not Issued	159	01/09/2001	POLYPODAL CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>60260615</u></a>	Not Issued	159	01/09/2001	TRIPODAL POLYAMINOPHOSPHONATES USEFUL FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>60216396</u></a>	Not	159	07/06/2000	STABLE RADIOPHARMACEUTICAL	LIU,

	Issued			COMPOSITIONS AND METHODS FOR PREPARATION THEREOF	SHUANG
<u>60213206</u>	Not Issued	159	06/21/2000	VITROVITRONECTIN RECEPTOR ANTAGONIST PHARMACEUTICALS	LIU, SHUANG
<u>60195235</u>	Not Issued	159	04/07/2000	NOVEL TERNARY LIGAND COMPLEXES USEFUL AS RADIOPHARMACEUTICALS	LIU, SHUANG
<u>60195234</u>	Not Issued	159	04/07/2000	MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<u>60153512</u>	Not Issued	159	09/13/1999	MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<u>60112715</u>	Not Issued	159	12/18/1998	PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS	LIU, SHUANG
<u>60080150</u>	Not Issued	159	03/31/1998	METALLOPHARMACEUTICALS FOR THE IMAGING AND TREATMENT OF CANCER	LIU, SHUANG
<u>60013360</u>	Not Issued	159	03/13/1996	TERNARY RADIOPHARMACEUTICAL COMPLEXES	LIU, SHUANG
<u>10918826</u>	Not Issued	020	08/13/2004	SUBSTITUTED PYRIDINONES	LIU, SHUANG
<u>10876893</u>	Not Issued	030	06/25/2004	POLYPODAL CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<u>10864857</u>	Not Issued	030	06/09/2004	CHELANTS AND MACROCYCLIC METAL COMPLEX RADIOPHARMACEUTICALS THEREOF	LIU, SHUANG
<u>10864792</u>	Not Issued	020	06/09/2004	CHELANTS AND MACROCYCLIC METAL COMPLEX RADIOPHARMACEUTICALS THEREOF	LIU, SHUANG
<u>10803724</u>	Not Issued	030	03/18/2004	N-SUBSTITUTED 3-HYDROXY-4-PYRIDINONES AND PHARMACEUTICALS CONTAINING THEREOF	LIU, SHUANG
<u>10742494</u>	Not Issued	030	12/19/2003	ACYCLIC PYRAZOLE COMPOUNDS FOR THE INHIBITION OF MITOGEN ACTIVATED PROTEIN KINASE ACTIVATED PROTEIN KINASE-2	LIU, SHUANG
<u>10663090</u>	Not Issued	092	09/15/2003	MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<u>10641688</u>	Not Issued	092	08/14/2003	LABELED MACROPHAGE SCAVENGER RECEPTOR ANTAGONISTS FOR IMAGING	LIU, SHUANG

				ATHEROSCLEROSIS AND VULNERABLE PLAQUE	
<a href="#"><u>10622246</u></a>	Not Issued	041	07/18/2003	PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS	LIU, SHUANG
<a href="#"><u>10467815</u></a>	Not Issued	020	08/12/2003	DIGITAL AUDIO PROCESSOR	LIU, SHUANG MING
<a href="#"><u>10367987</u></a>	Not Issued	041	02/14/2003	SUBSTITUTED PYRIDINONES	LIU, SHUANG
<a href="#"><u>10358835</u></a>	6825204	150	02/05/2003	N-SUBSTITUTED 3-HYDROXY-4-PYRIDINONES AND PHARMACEUTICALS CONTAINING THEREOF	LIU, SHUANG
<a href="#"><u>10342081</u></a>	6800273	150	01/14/2003	PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS	LIU, SHUANG
<a href="#"><u>10151663</u></a>	Not Issued	061	05/20/2002	RADIOPHARMACEUTICALS FOR IMAGING INFECTION AND INFLAMMATION	LIU, SHUANG
<a href="#"><u>10109374</u></a>	Not Issued	041	03/27/2002	RADIOPHARMACEUTICALS FOR IMAGING INFECTION AND INFLAMMATION	LIU, SHUANG
<a href="#"><u>10081258</u></a>	6713042	150	02/22/2002	ASCORBIC ACID ANALOGS FOR METALLORADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>10080974</u></a>	Not Issued	095	02/22/2002	LABELED MACROPHAGE SCAVENGER RECEPTOR ANTAGONISTS FOR IMAGING ATHEROSCLEROSIS AND VULNERABLE PLAQUE	LIU, SHUANG
<a href="#"><u>10033770</u></a>	6776977	150	12/27/2001	POLYPODAL CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>10033769</u></a>	Not Issued	041	12/27/2001	POLYPODAL CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>10033765</u></a>	6517814	150	12/27/2001	NEW MACROCYCLIC CHELANTS USEFUL FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>09899629</u></a>	Not Issued	121	07/05/2001	STABLE RADIOPHARMACEUTICAL COMPOSITIONS AND METHODS FOR PREPARATION THEREOF	LIU, SHUANG
<a href="#"><u>09826549</u></a>	6565828	150	04/05/2001	MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>09826449</u></a>	6534038	150	04/05/2001	TERNARY LIGAND COMPLEXES USEFUL AS	LIU, SHUANG

RADIOPHARMACEUTICALS					
<a href="#"><u>09660377</u></a>	<a href="#"><u>6685914</u></a>	150	09/12/2000	MACROCYCLIC CHELANTS FOR METALLOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>09599295</u></a>	<a href="#"><u>6537520</u></a>	150	06/21/2000	PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS	LIU, SHUANG
<a href="#"><u>09281474</u></a>	Not Issued	041	03/30/1999	PHARMACEUTICALS FOR THE IMAGING OF ANGIOGENIC DISORDERS	LIU, SHUANG
<a href="#"><u>09277936</u></a>	<a href="#"><u>6251364</u></a>	150	03/29/1999	NOVEL TERNARY LIGAND COMPLEXES USEFUL AS RADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>09013320</u></a>	<a href="#"><u>6010679</u></a>	150	01/26/1998	TERNARY RADIOPHARMACEUTICAL COMPLEXES	LIU, SHUANG
<a href="#"><u>08999400</u></a>	<a href="#"><u>6022523</u></a>	150	12/29/1997	RADIOLABELED PLATELET GPIIB/III $\alpha$ RECEPTOR ANTAGONISTS AS IMAGING AGENTS FOR THE DIAGNOSIS OF THROMBOEMBOLIC DISORDERS	LIU, SHUANG
<a href="#"><u>08956313</u></a>	<a href="#"><u>6015904</u></a>	150	10/23/1997	STABLE REAGENTS FOR THE PREPARATION OF RADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>08943659</u></a>	<a href="#"><u>6416733</u></a>	150	10/03/1997	RADIOPHARMACEUTICALS FOR IMAGING INFECTION AND INFLAMMATION	LIU, SHUANG
<a href="#"><u>08864586</u></a>	<a href="#"><u>6403054</u></a>	150	05/28/1997	NEW TERNARY LIGAND COMPLEXES USEFUL AS RADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>08476296</u></a>	<a href="#"><u>5750088</u></a>	150	06/07/1995	STABLE HYDRAZONES LINKED TO A PEPTIDE MOIETY AS REAGENTS FOR THE PREPARATION OF RADIOPHARMACEUTICALS	LIU, SHUANG
<a href="#"><u>08218861</u></a>	<a href="#"><u>5879657</u></a>	150	03/28/1994	RADIOLABELED PLATELET GPIIB/III $\alpha$ RECEPTOR ANTAGONISTS AS IMAGING AGENTS FOR THE DIAGNOSIS OF THROMBOEMBOLIC DISORDERS	LIU, SHUANG

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